REMARKS

Claims 1-22 were pending in the application, with claims 1-5 and 9-22 withdrawn from consideration. Claims 9-12 and 14-22 are cancelled herein without prejudice.

The title of the application is deleted herein and replaced with the title "Methods of Detecting Colon Cancer Cells."

Claim 6 is amended to recite a method for assessing the phenotype of a colon cell comprising: detecting expression of a gene product in a test colon cell sample, wherein the gene product is encoded by a gene defined by SEQ ID NO:22; and comparing a level of expression of the gene product in the test colon cell sample with a level of expression of the gene product in a control colon cell sample; wherein a test colon cell sample with a level of expression of the gene product increased at least 2-fold compared to the control colon cell sample is indicative of a colon cell with a cancerous phenotype.

In addition, new claims 23-28 are added herein. Claims 23 and 24 depend from claim 6 and recite, respectively, that a test colon cell sample with a level of expression of the gene product increased at least 2.5-fold or at least 5-fold compared to the control colon cell sample is indicative of a colon cell with a cancerous phenotype. Support for these amendments can be found in Applicants' specification at, for example, page 6, paragraph [0022], page 50 paragraph [00158], and page 54, paragraph [00170], which disclose that a differentially expressed polynucleotide can be found at a level that is, *inter alia*, at least about 2-fold higher (e.g., about 2.5-fold higher or about 5-fold higher) in a cancerous colon cell than in a cell of the same cell type that is not cancerous. These paragraphs also disclose that matched normal colon tissue was used as a control in the experiments carried out by the inventors. Claim 25 depends from claim 7, and recites that the detecting comprises contacting the test colon cell sample with a polynucleotide that specifically hybridizes to the RNA transcript. Support for claim 25 can be found, for example, at pages 28 and 29, paragraphs [0094] to [0097]. Claim 26 depends from claim 8, and recites that the detecting comprises contacting the test colon cell sample with a probe specific for the polypeptide. Claim 27 recites that the probe is an antibody, and claim 28 recites that the antibody is detectably labeled. Support for claims 26-28 can be found in

Applicants' specification at, for example, pages 26 and 27, paragraphs [0087] through [0090]. Thus, no new matter has been added.

Upon entry of this amendment, claims 6-8 and 23-28 will be pending.

Objections

The Office objected to the title of the invention, alleging that it is not descriptive. Although Applicants do not agree, the title of the application has been amended to read "Methods of Detecting Colon Cancer Cells." In light of this amendment, Applicants respectfully request withdrawal of the objection to the title.

Rejection under 35 U.S.C. §112, first paragraph

Claims 6-8 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to adequately enable the pending claims. The Office alleged that for various reasons, a person of skill in the art would not be able to conclude that a comparison of gene expression in a test cell vs. a control cell would be indicative of a cancerous state in the test cell. First, the Office asserted that the control cell sample as recited in claim 6 is not necessarily from colon, and that a person of skill in the art would not be able to make sound conclusions while comparing a control sample from a different organ, such as the heart, to a test sample from colon. The Office also asserted that comparing expression levels alone does not necessarily indicate the cancerous state of a test sample, as any variation between a test sample and control sample may be due to random sampling error. Thus, the Office alleged that the quantity of experimentation required to verify that SEQ ID NO: 22 represents a valid indicator of a cancerous state of a test colon cell sample appears to be undue.

Applicants disagree. To further prosecution, however, Applicants have amended claim 6 to recite that the control cell sample is a colon cell sample, and also to recite that a test colon cell sample with a level of expression of the gene product increased at least 2-fold compared to the control colon cell sample is indicative of a colon cell with a cancerous phenotype.

The standard for enablement is met so long as one of skill in the art can make and use the claimed invention without undue experimentation. The present claims are fully enabled, as no

undue experimentation would be required for a skilled artisan to carry out the recited methods. First, the present claims require that the control cell sample is a colon cell sample. Second, Applicants' specification clearly discloses that the level of SEQ ID NO:22 was increased in colon cancer cells as compared to control colon cells. *See*, for example, page 54, paragraph [00170], and Table 6, which disclose that expression levels of SEQ ID NO:22 were at least 2-fold greater in colon tumor samples than matched normal tissue in 66.7% of patients tested. In fact, Table 6 discloses that expression levels of SEQ ID NO:22 were at least 2.5-fold greater in colon tumor samples than matched normal tissue in 66.7% of patients tested, and at least 5-fold greater in colon tumor samples that matched normal tissue in 51.5% of patients tested. Thus, it is clear from Applicants' specification that SEQ ID NO:22 is a valid colon cancer indicator. Any experimentation required for a person of skill in the art to conclude that a cancerous state is present in a test colon cell sample in which expression of SEQ ID NO:22 is increased at least 2-fold compared to a control colon cell sample would be routine, and not undue. As such, the present claims are fully enabled.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 6-8 under 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §112, second paragraph

Claims 6-8 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Office alleged that the preamble of claim 6 recites assessing the cancerous phenotype of a colon cell, but the method steps do not recite any phenotypic limitations. Therefore, the Office asserted that it is unclear if the preamble or the body of the claim is controlling the metes and bounds of the claim. The Office also asserted that claims 7 and 8 recite "expression of the gene," but that there is insufficient antecedent basis for this limitation because while there is previous mention of expression of a gene product, there is no previous mention of a gene.

Claim 6 has been amended to recite that a test colon cell sample with a level of expression of the gene product increased at least 2-fold compared to the control colon cell

sample is indicative of a colon cell with a cancerous phenotype. Thus, the body of the claim is consistent with the preamble.

Applicants disagree with the rejection of claims 7 and 8. Claim 6 recites that the gene product is encoded by a gene defined by SEQ ID NO:22, and thus provides sufficient antecedent basis for the recitation of "expression of the gene" in claims 7 and 8.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 6-8 under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §102

Claims 6-8 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,500,938 (the Au-Young *et al.* patent). The Office asserted that the Au-Young patent discloses a composition comprising at least a portion of a sequence selected from the group consisting of SEQ ID Nos:1-1490, and that SEQ ID NO:249 is identical to SEQ ID NO:22 of the instant claim 6. The Office further alleged that the Au-Young *et al.* patent discloses using non-tumorous colon tissue and diseased colon tissue to assess differences in gene expression, and using expression profiles that can reflect detectable levels of a plurality of target polynucleotides in a sample for diagnosing cancer. Thus, the Office alleged that the Au-Young *et al.* patent anticipates claims 6-8.

Applicants respectfully disagree, as the Au-Young *et al.* patent fails to disclose each and every limitation of the presently pending claims. As noted above, present claim 6 recites that a test colon cell sample with a level of expression of the gene product increased at least 2-fold compared to the control colon cell sample is indicative of a colon cell with a cancerous phenotype. At no point does the Au-Young *et al.* patent disclose that a 2-fold increase in the level of expression of SEQ ID NO:249 set forth therein is indicative of a cancerous phenotype in a colon cell. Further, the Au-Young *et al.* patent contains no disclosure that a 2.5-fold or 5-fold increase in the level of expression of SEQ ID NO:249 is indicative of a cancerous phenotype in a colon cell. As such, the present claims are novel over the Au-Young *et al.* patent.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 6-8 under 35 U.S.C. § 102(e).

CONCLUSION

The foregoing represents a *bona fide* attempt to advance the present application to allowance. Applicants submit that claims 6-8 and 23-28 are in condition for allowance, which action is respectfully requested. The Examiner is invited to telephone the undersigned agent if such would further prosecution.

Please charge $450 for the extension of time, and apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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